Pre-clinical diabetic cardiomyopathy: prevalence, screening, and outcome

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Abstract: AIMS: Diabetic cardiomyopathy, characterized by left ventricular (LV) dysfunction and LV hypertrophy independent of myocardial ischaemia and hypertension, could contribute to the increased life-time risk of congestive heart failure seen in patients with diabetes. We assessed prospectively the prevalence, effectiveness of screening methods [brain natriuretic peptide (BNP) and C-reactive protein in combination with clinical parameters], and outcome of pre-clinical diabetic cardiomyopathy. METHODS AND RESULTS: We studied 100 adults (mean age 57.4 +/- 10.2 years, 44% females) with diabetes and no previous evidence of structural heart disease. By echocardiography, diabetic cardiomyopathy was present in 48% of patients. Screening with combinations of clinical parameters (gender, systolic blood pressure, and body mass index), but not BNP, resulted in high negative predictive values for diabetic cardiomyopathy. During a mean follow-up of 48.5 +/- 9.0 months, in the groups with and without diabetic cardiomyopathy, 12.5 vs. 3.9% ($P < 0.2$) patients died or experienced cardiovascular events and 37.5 vs. 9.6% ($P < 0.002$) had a deterioration in NYHA functional class. Overall event-free survival was 54 vs. 87% ($P = 0.001$) in the groups with and without diabetic cardiomyopathy, respectively. Brain natriuretic peptide was an independent predictor of events [odds ratio 3.5 (1.1-10.9), $P = 0.02$]. CONCLUSION: Pre-clinical diabetic cardiomyopathy is common. Screening with combinations of simple clinical parameters, but not BNP, can be useful to identify those patients needing further evaluation. Patients with pre-clinical diabetic cardiomyopathy are at increased risk for functional deterioration and possibly cardiovascular events during follow-up. Brain natriuretic peptide was shown to be an independent predictor of future events.

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Preclinical diabetic cardiomyopathy: prevalence, screening and outcome

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Abstract

Aims. Diabetic cardiomyopathy, characterized by left ventricular (LV) dysfunction and hypertrophy (LVH) independent of myocardial ischemia and hypertension could contribute to the increased life-time risk of congestive heart failure seen in patients with diabetes. We assessed prospectively prevalence, screening methods (brain natriuretic peptide (BNP) and CRP in combination with clinical parameters) and outcome of preclinical diabetic cardiomyopathy.

Methods and results. We studied 100 adults (mean age 57.4±10.2 years, 44% females) with diabetes and no previous evidence of structural heart disease. By echocardiography, diabetic cardiomyopathy was present in 48% of patients. Screening with combinations of clinical parameters (gender, systolic blood pressure and body mass index), but not BNP, resulted in high negative predictive values for diabetic cardiomyopathy. During a mean follow-up of 48.5±9.0 months 12.5% vs 3.9% ($p<0.2$) experienced death or cardiovascular events and 37.5% versus 9.6% ($p<0.002$) a deterioration of NYHA functional class with an overall event-free survival of 54 versus 87% ($p=0.001$) in the groups with and without diabetic cardiomyopathy. BNP was an independent predictor of events (OR 3.5 (1.1-10.9), $p=0.02$).

Conclusions. Preclinical diabetic cardiomyopathy is common. Screening with combinations of simple clinical parameters, but not BNP, can be useful to identify those patients needing further evaluation. Patients with preclinical diabetic cardiomyopathy are at increased risk for functional deterioration and possibly cardiovascular events during follow-up. BNP was shown to be an independent predictor of future events.

Key words. Diabetes, left ventricular dysfunction, left ventricular hypertrophy, diabetic cardiomyopathy, brain natriuretic peptide, outcome

Introduction

Cardiovascular complications, mainly as a consequence of premature and accelerated coronary disease, are the leading cause of morbidity and mortality in patients with diabetes (1). In addition, there is an increased life-time risk of congestive heart failure and these patients are over-represented in large heart failure databases (2). Clinical and experimental studies have supported the concept of a diabetic cardiomyopathy with functional, biochemical and morphological myocardial abnormalities independent of myocardial ischemia and hypertension (3) leading to left ventricular (LV) dysfunction and hypertrophy (LVH) in a substantial proportion of type I and II diabetics (4-5). Still, only limited information is available regarding the prevalence and outcome of preclinical diabetic cardiomyopathy.

Besides coronary disease, LV dysfunction and LVH are the most promising therapeutic targets to reduce cardiac morbidity and mortality in diabetic patients. Echocardiography, the cornerstone of diagnostic evaluation for LV dysfunction and LVH, is currently not performed routinely in diabetic patients because of limited availability and relatively high cost. Therefore, a simple test to detect those patients with the highest likelihood of LV dysfunction and LVH requiring further evaluation would be attractive. Brain natriuretic peptide (BNP) and high sensitivity c-reactive protein (hs-CRP) reflecting hemodynamic stress and inflammation, respectively, are potential biochemical screening tests for this purpose (6-10).

Thus, the objectives of this pilot study in diabetic patients without previously known heart disease were: first, to assess the prevalence of systolic and diastolic LV dysfunction and LVH as diagnosed by comprehensive Doppler-echocardiography; second, to evaluate the usefulness of BNP and hs-CRP alone or in combination with clinical parameters as screening tools; and third, to study the outcome of preclinical diabetic cardiomyopathy.

Methods

The investigation conforms with the principles outlined in the Declaration of Helsinki, the research protocol was approved by the local Ethics Committee and written informed consent was obtained by all patients prior to inclusion in the study.

Patients. We recruited prospectively from our diabetes outpatient clinic 100 adults with type I or II diabetes treated with insulin and/or oral antidiabetics who were in sinus rhythm. Exclusion criteria included: previous diagnosis, symptoms or signs of heart failure, coronary or other structural heart disease; untreated hypertension; acute infections; alcohol or drug abuse and elevated serum creatinine. After a detailed history and physical examination including the Framingham heart failure criteria (11), nonfasting venous blood samples were obtained, a standard 12-lead ECG was acquired and a Doppler-echocardiography was performed on the same day.

Laboratory analysis. Plasma BNP concentrations were measured with the Biosite® Access BNP-immunoassay and hs-CRP was determined by immunonephelometry on the Beckman Image Nephelometer. The detection limits are 5 pg/ml for BNP and 0.06 mg/l for hs-CRP, respectively. In addition, serum creatinine, glucose, hemoglobin A1c, total cholesterol, LDL-cholesterol and triglycerides were measured by standard techniques.

Echocardiography. Doppler-echocardiography was performed by one of two cardiologists (SK, PR) blinded to laboratory results using a Sonos 5500 system (Philips, Eindhoven, the Netherlands).

Two-dimensional echocardiography and M-mode measurements were obtained in standard fashion. LV ejection fraction was measured using a modified Simpson's rule algorithm or, if volumes could not be quantified due to limited image quality, by visual assessment. LV mass

was determined using Devereux's formula (12). Each participant underwent pulsed-wave Doppler examination of mitral and pulmonary venous inflow and Doppler tissue imaging of the mitral anulus. Peak values of mitral E- and A-wave velocities and E/A ratios before and during Valsalva maneuver, A-wave duration (Adur) and deceleration time of the E-wave (DT) were recorded and ΔE/A was calculated as E/A before – E/A during Valsalva maneuver. Pulmonary venous flow measurements included peak systolic (S) and diastolic (D) flow velocities and duration of atrial reversal flow (ARdur). In addition, tissue Doppler imaging of the mitral anulus was obtained in the apical four-chamber view and the early diastolic peak velocity (E') was recorded. Mean heart rate during the Doppler study was 75±11 beats / minute.

LV systolic dysfunction was defined as LV ejection fraction of <45 % and LV end-diastolic internal dimension index of >3.2 cm/m^2 or LV end-diastolic volume index of >102 ml/m^2 (13). Diastolic dysfunction was categorized as mild, defined as impaired relaxation without evidence of increased filling pressures (E/A≤0.75, ΔE/A<0.5, E/e'<10, S>D, ARdur <Adur); moderate, defined as impaired relaxation associated with moderate elevation of filling pressures or pseudonormal filling (E/A>0.75-<1.50, DT>140 ms, ΔE/A≥0.5, E/e'≥10, S<D or ARdur>Adur+30ms); and severe, defined as advanced reduction in compliance or restrictive filling (E/A>1.5, DT<140ms, ΔE/A≥0.5 (reversible) or <0.5 (fixed), E/e'≥10, S<D or ARdur>Adur+30ms), as previously described (14). Participants with E/A>0.75 were required to have ≥2 additional Doppler criteria consistent with moderate or severe diastolic dysfunction to be so classified and were otherwise classified as indeterminate diastolic function. For further comparison, the groups with normal and indeterminate function were combined. LVH was defined as LV mass index ≥131 g/m^2 for men and ≥100 g/m^2 for women (12).

ECG. Electrocardiographic LVH was diagnosed with the Sokolow-Lyons index (SV_1 + RV_{5-6}) >38 mm or the Cornell modified index ((RaVL + SV_3) x QRS duration in men; (RaVL + SV_3 + 6 mm) x QRS duration in women)) > 2440 mm x ms (15).

Definition of preclinical diabetic cardiomypathy. Presence of left ventricular dysfunction and / or LVH by Doppler-echocardiography in type I or II diabetics treated with insulin and / or oral antidiabetics in the absence of clinical evidence of coronary / other structural heart disease or untreated hypertension.

Outcome. Patients were followed every 6 months for a minimum of 3 years by structured telephone interview using a self-designed flow-sheet with the events in question defined according to standard clinical criteria. Medical records were reviewed in case of hospitalisation and referring physicians were contacted for additional information. Besides NYHA functional class (limitations of functional capacity due to shortness of breath as compared to the previous observation period) the following events were recorded: death (cardiac/noncardiac), acute coronary syndrome, hospitalisation for cardiac reasons and new diagnosis of heart failure. The physicians collecting the follow-up data (SK, RG, PR) were blinded to laboratory and echocardiographic results.

Statistical analysis. Values are expressed as mean ±1 SD, median (IQR), or frequencies as indicated. Between-group differences were compared using the chi-square test, Fisher's exact test, or Student's t-test, as appropriate. Because BNP and hs-CRP values were not normally distributed, the Mann-Whitney test was used for comparison. Receiver-operator-characteristic (ROC) curves were constructed to calculate the predictive values of BNP and hs-CRP for the diagnosis of LV dysfunction, LVH and diabetic cardiomyopathy and the values with best diagnostic accuracies where obtained. A multiple logistic regression model was used for evaluating the ability of biochemical markers to identify LV dysfunction, LVH and diabetic cardiomyopathy over and above the information provided by other indicators. Sensitivity, specificity, positive (PPV) and negative (NPV) predictive values were calculated for independent

predictors. The effect of diabetic cardiomyopathy on outcome defined as events (see above), deterioraton of NYHA functional class and both these outcomes combined, was analyzed with the Kaplan-Meier method using log rank (Mantel-Cox) test to assess for equality of survival curves. Logistic regression was employed to calculate relative risks (95% CI) for selected outcome variables with sufficient numbers of events and to evaluate the ability of BNP, clinical and echocardiogaphic parameters to predict prognosis. Statistical analyses were performed using commercially available software (Statview version 5.0, SAS Institute Inc., Cary, North Carolina and SPSS version 12.0, SPSS Inc., Chicago, Illinois). A p-value of <0.05 was considered to indicate statistical significance.

Results

Prevalence. Baseline characteristics of the total study population and the groups with and without diastolic dysfunction, LVH and diabetic cardiomyopathy are shown in Table 1. Diastolic function was normal in 42 (42%), abnormal in 38 (38%) and indeterminate in the remaining 20 (20%) patients. In those with abnormal diastolic function, severity was classified as mild in 27 (71%), moderate in 10 (26%) and severe in 1 (3%) patients. LVH was diagnosed in 24 patients (24%). No patient showed systolic dysfunction, the mean LV ejection fraction was 62±6%. Forty-eight patients (48%) had diabetic cardiomyopathy.

Screening. Median (IQR) BNP values in patients with normal, indeterminate and abnormal diastolic function were 21 (18), 30 (39) and 44 (58) pg/ml respectively (p=0.0003 between normal and abnormal function). Patients with mild, moderate and severe diastolic dysfunction showed median BNP values of 36 (55), 57 (60) and 167 pg/ml respectively (p=0.01 normal diastolic function vs mild and p=0.0011 normal vs moderate dysfunction). There was also a significant difference in median BNP values between patients with and without LVH (37 (54)

vs 29 (30) pg/ml; p<0.05) and in those with versus without diabetic cardiomyopathy (37 (50) vs 24 (22) pg/ml, p=0.0033). Values of hs-CRP were not significantly different in all those subgroups (data not shown).

The areas under the curve for the ROC analyses with BNP used to detect diastolic dysfunction, LVH and diabetic cardiomyopathy were 0.70 (0.59-0.81, p=0.001), 0.63 (0.51-0.76, p<0.05) and 0.67 (0.57-0.78, p=0.003) respectively. A BNP cutoff value of 34 pg/ml had a sensitivity of 66%, 58% and 58%, a specificity of 71%, 62% and 71%, a PPV of 58%, 33% and 65% and a NPV of 77%, 83% and 65% to detect any diastolic dysfunction, LVH and diabetic cardiomyopathy.

By multivariate logistic regression BNP, hypertension, systolic blood pressure were independent predictors of diastolic dysfunction and female gender, systolic blood pressure, body mass index (BMI) of diabetic cardiomyopathy, respectively, whereas female gender remained as only independent predictor of LVH (data not shown). Sensitivities, specificities, NPV and PPV of the independent variables alone or in combination are shown in Table 2 and the clinical implications for screening based on these results in Table 3. BNP alone was only moderately useful to detect diastolic dysfunction alone whereas combinations of the clinical parameters listed above resulted in high negative predictive values for diabetic cardiomyopathy.

Outcome. During a mean follow-up of 48.5±9.0 months (≥36 months except for one patient who moved to another country after 24 months) the following events were observed in the groups with and without diabetic cardiomyopathy: noncardiac deaths 2 versus 1, acute coronary syndrome 2 versus 1, hospitalisation for cardiac reasons 4 versus 1 and new diagnosis of heart failure 2 versus 0; the number of patients with events was not significantly different between the groups (6 (12.5%) vs 2 (3.9%), p<0.2)). Significantly more patients with diabetic cardiomyopathy experienced a deterioration of NYHA functional class (18 (37.5%) versus 5 (9.6%), p<0.002; OR 4.5 (1.7-12.3), p=0.0009). The combined event-free survival was 54 ver-

sus 87% (OR 3.8 (1.6-8.9), p=0.001) in the groups with and without diabetic cardiomyopathy as shown in figure 1. In addition, by univariate analysis, events were more likely to occur in patients with higher BNP (p=0.006) and older age (p<0.05), functional deterioration with higher BMI (p<0.003) and female gender (p<0.002) and the combined endpoint with higher BNP (p<0.006) and hs-CRP (p<0.04), higher BMI (p<0.03) older age (p<0.03) as well as female gender (p=0.007). BNP remained an independent predictor of events (OR 3.5 (1.1-10.9), p=0.02), female gender (OR 3.6 (1.2-10.8), p<0.02) and diabetic cardiomyopathy (OR 3.7 (1.1-11.0), p<0.03) of functional deterioration and diabetic cardiomypathy alone (OR 3.5 (1.1-10.9), p<0.03) of the combined endpoint by multivariate logistic regression.

Discussion

This study demonstrates that echocardiographic evidence for diabetic cardiomyopathy is common, especially in women, even in diabetic patients without previously known heart disease. Screening with combinations of simple clinical parameters, but not BNP alone, can be useful to identify those patients needing further evaluation. This is of clinical importance as patients with preclinical diabetic cardiomyopathy are at increased risk for functional deterioration and possibly cardiovascular events during follow-up. BNP was shown to be an independant predictor of future events.

Definition of diabetic cardiomyopathy. As mentioned earlier, in a strict sense, diabetic cardiomyopathy has been defined as left ventricular dysfunction and/or hypertrophy independent of coronary disease and hypertension. However, a number of variations of this definition have been used in clinical studies. In the present analysis, patients did not have a history or symptoms suggestive of coronary disease and therefore no stress testing or coronary angiography were performed in the context of the study. Synergy between diabetes and hypertension is a

very frequent coincidence and there is evidence that their effect on the heart are similar, independent and synergistic (16). We decided not to exclude patients with hypertension if they were treated for this condition to better reflect the typical clinical scenario.

Prevalence of diabetic cardiomyopathy. Numerous previous studies, using mainly Doppler echocardiography, have attempted to determine diastolic function in subjects with diabetes. Differences in the patient populations studied and in the definition of diastolic dysfunction most likely accounted for the highly varying prevalences of 30-75% reported in the literature (17-24). In our clinically well characterized population without evidence of heart disease, diastolic dysfunction was observed in 38%. This prevalence is higher than in the general population. Others, using the same (14) or a comparable (25) definition of diastolic dysfunction found a prevalence of diastolic dysfunction in large community based populations of 27.4% and 29.1%, respectively. However, mean age was substantially higher in both reports as compared to our population and a history of coronary disease, a previous myocardial infarction, a reduced ejection fraction (14) and heart failure (25) were not exclusion criteria, making a direct comparison with our results difficult.

The prevalence of LVH in the general population is mainly dependent on age and the presence of hypertension, varying from 6% to over 50% in several large series (26-28). Increased left ventricular mass and wall thickness have also consistently been documented in diabetics (4, 5, 29). In the present study 24% had echocardiographic LVH. A higher prevalence of 43% has been described in unselected older patients with diabetes using the same definition for LVH in the only other publication reporting prevalence (23).

Diastolic dysfunction and/or LVH, as structural and functional evidence for preclinical diabetic cardiomyopathy, were present in 48% of our population. Remarkably, the prevalence of this entity was strikingly high in women in our study. Heart failure with preserved ejection fraction is commonly believed to be more common in women than in men but data regarding

gender differences in diabetic cardiomyopathy are rare in the literature. Only in the Framingham study (5), an independant association was reported between diabetes and left ventricular mass in women only. Clearly, this issue merits further evaluation.

Screening for diabetic cardiomyopathy. BNP was reported to reliably predict diastolic dysfunction in diabetic patients with and without clinical indications for echocardiography but, unfortunately, only little clinical information was provided in this study (30). In contrast, in a number of large, community-based populations BNP proved to be a suboptimal screening test to detect preclinical LV dysfunction or LVH (6-8). In addition, BNP was not useful to predict LV dysfunction in asymptomatic patients with diabetes in two small reports (31-32). In accordance with these results, BNP was moderately predictive for the presence of LV diastolic dysfunction but not for LVH or diabetic cardiomyopathy in the present analysis. The combination of clinical parameters, mainly characteristics of the metabolic syndrome, resulted in high negative predictive values for diastolic dysfunction and diabetic cardiomyopathy. A substantial proportion of the diabetic population would need an echocardiogram with this approach, around one third of these would be negative but very few patients with diabetic cardiomyopathy would be missed.

Elevated hs-CRP levels have been shown to be associated with LVH in patients with type 2 diabetes (9) and have been identified as markers of future heart failure in the Framingham population (10). Hs-CRP alone or in combination with BNP or clinical parameters did not prove to be useful as a diagnostic or prognostic marker regarding diabetic cardiomyopathy in our study.

Outcome of diabetic cardiomyopathy. Our finding that patients with preclinical diabetic cardiomyopathy are at increased risk for adverse outcome driven mainly by symptomatic deterioration may be seen as not surprising in view of the well established prognostic role of LVH

(33) and diastolic dysfunction (14) regarding cardiovascular morbidity and all-cause mortality. However, to our knowledge, this has not been reported yet. We found an almost 4-fold increased risk in patients with evidence for preclinical diabetic cardiomyopathy, underscoring the need for proper diagnostics and appropriate treatment in this population. In accordance with a recent report (34), patients with increased BNP levels are at particular risk. The results presented in this study may help to identify these patients.

Limitations: A number of limitations apply to this study. First, no power calculation to determine sample size was performed because prevalence and outcome of preclinical diabetic cardiomyopathy were unknown at the time the study was designed. It can therefore not be excluded that the study was underpowered to detect differences regarding hard clinical endpoints. Second, silent coronary artery disease may have been the cause for some of the follow-up events in addition to the three cases of acute coronary syndrome. Third, since arterial hypertension and systolic blood pressure were independently associated with diastolic dysfunction, hypertensive heart disease may have contributed to the echocardiographic findings besides diabetic cardiomyopathy. However, this does not limit the clinical implications of our study.

Conclusions. The prevalence of preclinical diabetic cardiomyopathy is high in diabetics without known structural heart disease and is associated with adverse outcome. Screening of diabetics based on combinations of simple clinical parameters, such as systolic blood pressure, BMI and gender can be useful to select those patients needing further evaluation with echocardiography. BNP alone was not a powerful screening test for diabetic cardiomyopathy but was shown to be an independant predictor of future events. Whether the structural and functional abnormalities of preclinical diabetic cardiomyopathy can be reversed and the outcome improved with treatment remains to be determined.

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Figure legends

Figure 1. Event-free survival (death, acute coronary syndrome, hospitalisation for cardiac reasons, new diagnosis of heart failure, ≥1 increase in NYHA functional class) in patients with and without diabetic cardiomyopathy.

Table 1. Baseline characteristics

Parameter	**Total population** (n=100)	**Diastolic function**			**LVH**			**diabetic cardiomyopathy**		
		normal (n=62)	**abnormal** (n=38)	**p-value**	**absent** (n=76)	**present** (n=24)	**p-value**	**absent** (n=52)	**present** (n=48)	**p-value**
Age (years)	57.4±10.2	54.3±9.4	62.4±9.3	<0.0001	56.0±9.9	61.6±9.9	<0.02	53.9±9.6	61.2±9.4	0.0002
Female gender (%)	44	32	63	<0.004	36	71	<0.005	27	63	0.0005
Typ II diabetes (%)	78	74	84		76	83		73	83	
Diabetes duration (years)	12.1±10.4	12.4±10.4	11.6±10.5		12.0±10.6	12.3±9.8		11.9±9.9	12.3±10.9	
Hemoglobin A1c (%)	7.4±0.9	7.4±0.9	7.3±0.9		7.3±0.9	7.5±0.9		7.5±1.0	7.2±0.9	
Hypertension* (%)	58	45	79	0.0009	59	54		48	69	<0.05
Systolic BP† (mmHg)	134±19	130±16	141±21	<0.003	132±18	140±21		130±17	139±19	<0.03
Diastolic BP (mmHg)	80±12	79±12	81±12		80±12	81±14		79±12	81±13	
Hyperlipidemia‡ (%)	79	73	89	<0.05	80	75		73	85	
Total cholesterol (mmol/l)	5.0±1.0	4.9±0.9	5.1±1.0		5.0±0.9	4.8±1.1		4.9±0.9	5.1±1.0	
LDL-cholesterol (mmol/l)	3.0±0.9	3.0±0.9	3.1±0.9		3.1±0.9	2.9±0.9		3.0±0.9	3.0±0.8	
Triglycerides (mmol/l)	2.5±1.4	2.4±1.5	2.7±1.4		2.5±1.5	2.7±1.3		2.3±1.5	2.8±1.4	
Current smoker (%)	33	36	29		37	21		39	27	
Family history§ (%)	20	21	18		20	21		17	23	

NYHA class I/II (%)	85/15		89/11	79/21			88/12	75/25			88/12	81/19	
Body mass index	30.1±5.2		29.5±5.0	31.1±5.3			29.5±5.1	32.0±5.2	<0.04		28.7±4.9	31.6±5.1	<0.005
Medication history													
Aspirin (%)	28		26	32			24	42			23	33	
ACE-I/ARB[‖] (%)	54		48	63			50	67			48	60	
Betablocker (%)	15		10	24			19	25			6	25	<0.02
Calcium antagonist (%)	12		5	24	<0.009		12	13			4	21	<0.02
Diuretic (%)	30		23	42	<0.05		30	30			27	33	
Statin (%)	43		44	43			45	38			48	38	
Insulin (%)	28		32	21			29	25			34	21	
Oral antidiabetic (%)	32		29	37			33	29			31	33	
Both (%)	40		39	42			38	46			35	46	
ECG LVH (%)	3		0	8			3	4			0	6	

[*]History of or current treatment for arterial hypertension; [†]blood pressure; ‡Statin treatment or total cholesterol >5 mmol/l or LDL-cholesterol >3 mmol/l; [§]family history of premature coronary artery disease; [‖]ACE-inhibitor/angiotensin receptor blocker.

Table 2.

Sensitivity, specificity, PPV and NPV of selected parameters to identify diastolic dysfunction, LVH and diabetic cardiomyopathy

Diastolic dysfunction

Parameter	Sensitivity	Specificity	PPV	NPV
1. Hypertension	79	55	52	81
2. SBP*>134 mmHg	63	72	59	75
3. BNP >34 pg/ml	66	71	58	77
1.+2.	87	46	50	85
1.+3.	100	39	50	100
2.+3.	84	46	49	82
1.+2.+3.	100	26	45	100

LVH

Parameter	Sensitivity	Specificity	PPV	NPV
Female gender	71	64	39	88

Diabetic cardiomyopathy

Parameter	Sensitivity	Specificity	PPV	NPV
1. Female gender	63	73	68	68
2. SBP >134 mmHg	60	76	71	67
3. †BMI>30.1	65	65	63	67
1.+2.	88	52	63	82
1.+3.	88	48	61	81
2.+3.	94	45	62	89

*Systolic blood pressure, †Body Mass Index.

Table 3.

Identification of diastolic dysfunction, LVH and diabetic cardiomyopathy: implications for screening

Diastolic dysfunction (prevalence 38%)

Parameter	% screened needing echo	% echos that are negative	% with disease missed
1. Hypertension	58	28	18
2. SBP[*] >134 mmHg	42	17	14
3. BNP >34 pg/ml	43	18	13
1.+2.	66	33	5
1.+3.	76	38	0
2.+3.	65	33	6
1.+2.+3.	84	46	0

Left ventricular hypertrophy (prevalence 24%)

Parameter	% screened needing echo	% echos that are negative	% with disease missed
Female gender	44	27	7

Diabetic cardiomyopathy (prevalence 48%)

Parameter	% screened needing echo	% echos that are negative	% with disease missed
1. Female gender	44	14	18
2. SBP[*] >134 mmHg	42	12	19
3. [†]BMI>30.1	49	18	17

1.+2.	67	25	6
1.+3.	69	27	6
2.+3.	74	28	3
1.+2.+3.	85	37	1

*Systolic blood pressure, †Body Mass Index.

Figure 1

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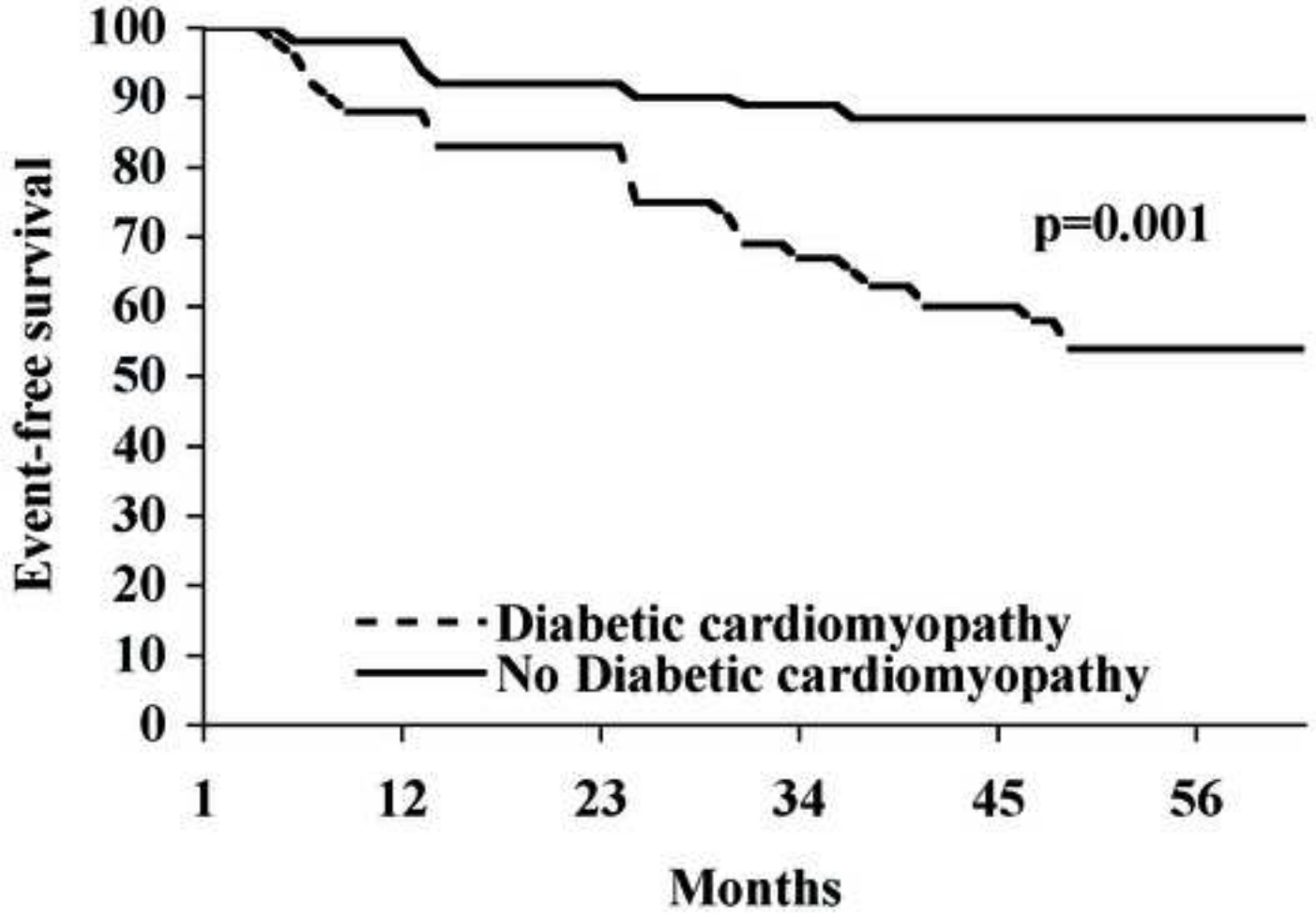

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